UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/077,027	02/15/2002	Douglas Richman	11068-008-999	2397

20583 7590 09/06/2005

JONES DAY
222 EAST 41ST ST
NEW YORK, NY 10017

EXAMINER	
WINKLER, ULRIKE	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 09/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/077,027	RICHMAN ET AL.	
	Examiner	Art Unit	
	Ulrike Winkler	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38,41,43-45,53-56 and 58-60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38,41,43-45,53-56 and 58-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Amendment filed April 02, 2004 in response to the Office Action of October 3, 2003 is acknowledged and has been entered. Claims 56, 58-60 have been added. Claims 38, 41, 43-45, 53-56-, 58-60 are pending and are currently being examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Drawings

The Office acknowledges the receipt of the revised Drawings.

Claim Rejections - 35 USC § 112

The rejection of claims 42, 45, 52 and 55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention **is withdrawn** in view of applicants cancellation or amendments to the claims.

Claim Rejections - 35 USC § 103

The rejection of the claims 38, 41, 43-45, 53-55 and newly added claims 56, 58-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gao et al. (Journal of Virology, 1996 ; see IDS), Petropoulos et al. (Antimicrobial Agents and Chemotherapy, April 200 ; see IDS) in view of Zhang et al. (Journal of Virology, 1999) **is maintained** for reasons of record. The rejection is maintained as evidenced by Fang et al. (Journal of Acquired Immune Deficiency

Syndromes and Human Retrovirology, 1996) the reference is cited for the purpose of rebutting applicants' argument.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

The test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

Applicants arguments is that that the cited references do not teach or suggest "HIV that uses a plurality of nucleic acids, each encoding an HIV envelope protein from HIV infecting the patients." Applicants arguments are not convincing because any time a viral nucleic acid sequences is amplified, using PCR, from a patient sample the nucleic acids represent a pool of those viral populations that are present in the patient. "HIV in plasma reflects the replication virus population at any point in time in vivo." (see Fang et al. ,1996, abstract). Different HIV-1 molecular clones may be cloned from a single clinical sample (see Fang et al. ,1996, page 353, column 1, 1st paragraph). "HIV-1 RNA genomes cloned directly from plasma provide in vivo

genetic information without selection from culture or provirus.... This method may be useful for studies of HIV genetic variation, evolution, pathogenesis, design of antiviral agents and vaccines and analysis of mechanisms of resistance." (see Fang et al. ,1996, page 357, column 1, 2nd paragraph).

Gao et al. teaches the use of a single round virus infectivity assay utilizing patient derived amplified envelope segments. The HIV nucleic acid is PCR amplified from patient derived PBMC cells and inserted into a plasmid construct. The viruses obtained from the samples revealed that several *env* genes represented mosaic *env* genes.

Petropoulos et al. teach a single cycle transfection assay with HIV vectors in which a patient sample can be tested for the sensitivity to a compound. In this assay the patient derived sample involves the polymerase gene. "The resistance test vectors (RTVs) were prepared as libraries (pools) in order to capture and preserve the PR and RT sequences." (see Petropoulos et al., 2000, page 921, 3rd paragraph). Thus, the reference teaches the use of a population of virus derived nucleic acids from a patients sample. The reference does not teach analyzing a patient derived *env* segment for their ability to infect new cells and for compounds that may inhibit the viral entry.

Zhang et al. teach an assay using a patient derived HIV *env* sequence in a pseudovirus construct. Here patient derived PBMC were cocultivated with normal PBMC in order to obtain replicating virus from patients. The RNA was extracted and the *env* genes were cloned into a plasmid. At this stage of the of the plasmid construction the plasmid represents the pool of viral sequences found in the RNA extract. Zhang et al screened these plasmids for function and those that produced a signal $\geq$ 100 times background were selected for further studies. Thus up to the

point of selecting the specific clones the references teaches looking a pool pseudoviral constructs representing the nucleic acids found in a patient sample.

It remains the position of the Office that it would have been obvious to one of ordinary skill in the art at the time the invention was filed to test patient derived anti-HIV antibody samples for their ability to neutralize viral entry (infectivity) into new cells. One having ordinary skill in the art would have been motivated to monitor the HIV status in a patient in order to provide the most directed treatment based on the HIV status in the patient. Different *env* sequences have different biological effects and ability to enter the host cells based on their ability to bind the host cell receptors. Determining if a patient derived virus has mutated to such a degree that it evades the neutralizing antibody response of the host and thereby requires a change in the treatment is desirable to optimize treatment protocols. Viruses that have diminished capacity to enter a new host cell are found in long terminal HIV survivors, indicating that reducing the ability of a particle to enter the next host cell will be beneficial for increasing the survival of an HIV infected person. The ordinary artisan at the time the invention was made would have known that envelope protein is an important player in the HIV viral life cycle. The envelope proteins are expressed on the surface of the viral particle and are involved in viral docking to the host cell via a cell surface receptor. The manipulation of retroviral sequences is well established, the prior art has shown that gag, *pol* and *env* can be expressed from separate plasmids and still result in virus particle formation. The prior art has taken envelope deleted HIV constructs and supplemented the construct with a plasmid carrying envelope from another stain of HIV or even another virus such as VSV-G. The Zhang et al. reference teaches testing an patient derived antibody sample with a patient derived envelope construct to determine if there

are mutation in the viral envelope during the infection results in a loss of binding to neutralizing antibody over the course of the infection. Optimizing experimental conditions, including the whether the nucleic acid constructs are to be found on an extrachromosomal plasmid or whether they are integrated into he host cell, falls within the skills of an ordinary artisan. If the location of the nucleic acid construct (integrated vs. expression plasmid based) produces an unexpected result, applicant needs to point out what the unexpected results are. Therefore, the instant invention is rejected in view of the cited art.

Conclusion

No claims allowed.

Applicant's arguments necessitated the ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 703-308-8294. The examiner can normally be reached M-F, 8:30 am - 5 pm. The examiner can also be reached via email [ulrike.winkler@uspto.gov].

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 703-308-4027.

The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 or for informal communications use 703-746-3162.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

ULRIKE WINKLER, PH.D.
PRIMARY EXAMINER 9/1/05